The Children's Mitochondrial Disease Network

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Mitochondrial Diseases
Information for Patients, Parents & Professionals

The Children's Mitochondrial Disease Network is the only Parental & Professional based Organization the UK & Europe Specializing in the Complexities of Mitochondrial Disorders.

What are Mitochondria ?

Mitochondria are small complex structures that exist in every cell of the body (except red blood cells). The mitochondrion has been called the 'powerhouse' of the cell because these tiny structures produce most of the energy that we all need to grow and live. Those organs in the body, which require a lot of energy to work properly, are particularly dependent on well functioning mitochondria. The most energy dependent organs are the brain, heart, skeletal muscle, kidney, endocrine glands and bone marrow and these are the organ systems commonly affected in mitochondrial diseases.

There are from one to several hundred mitochondria in each cell and each mitochondrion contains the complex molecules necessary to carry our energy making chemical reactions. Mitochondria perform many functions necessary for cell metabolism but the energy producing pathways are the most important. These pathways allow us to break down carbohydrate, fat and oxygen to live. Electrons from these food molecules are passed down a series of complex molecules called the electron transport chain. The final molecule in the chain, cytochrome oxidase, passes the electrons to oxygen

One unique feature of mitochondria is that they have their own DNA molecules, mitochondrial DNA, which carries the genes containing the genetic message for several critical components of the electron transport chain.

What is a Mitochondrial Disease ?

When enough mitochondria are not working correctly a disease may result. Mitochondrial diseases often involve the brain because of the tremendous energy requirements of the brain cells. Mitochondrial diseases are very variable in their features so called clinical heterogeneity.

The variability results from the fact that different organ systems contain different amounts of diseased mitochondria and only those tissues with a high percentage of diseased mitochondria will be functionally impaired. Mitochondrial diseases are whole body diseases but the exact features of the disease vary from one patient to another. Some patients will have predominantly brain disease or nerve disease. Others will have muscle disease (mitochondrial myopathy), cardiac disease (cardiomyopathies), endocrine, renal or bone marrow disease or a mixture of these and or other features.

Many mitochondrial diseases result in the accumulation of organic acids in the body. These are usually normal metabolic intermediates but when present in excess, the acidosis itself may be damaging or even life threatening. Lactic acid accumulation is a common problem in mitochondrial diseases.

We used to think of mitochondrial diseases as rare childhood disorders. Recently it has been discovered that many commoner disorders such as diabetes and ischemic heart disease have, in some cases, a mitochondrial basis. Also, diseases of aging such as Parkinson’s disease and Alzheimer’s disease may result in part from mitochondrial failure (The role that mitochondrial abnormalities play in the cause of these diseases remains to be established). In fact, the aging process itself may be due to a lifetime of damage to mitochondria through oxidative stress and accumulated damage to mitochondrial proteins and mitochondrial DNA.

Genetics of Mitochondrial Diseases?

Some mitochondrial diseases are clearly inherited and those involving mitochondrial DNA may be inherited through the maternal side of the family as almost all mitochondria come from the mother. Most inherited mitochondrial diseases however are so called nuclear DNA defects with inheritance from either the mother or father, or in most cases both. This latter inheritance pattern is termed autosomal recessive and in this case the risk of reoccurrence in a sibling is

25% or one in 1 in 4. Most childhood onset mitochondrial diseases are inherited although in some cases the affected child seems to be the only affected family member.

Diseases resulting from mitochondrial deletions of large parts of the mitochondrial DNA molecule are usually sporadic without other affected family members. Genetic counselling is complex for mitochondrial diseases.

Pre-natal testing is only available for a few disorders.

How are Mitochondrial Diseases diagnosed?

Because of the multiple organ systems involved and the variation in the age of onset, mitochondrial diseases may be difficult to recognize. Even within the same family the same disease may affect individuals differently. A severe childhood disease such as Leigh's syndrome may occur in the same family with later onset adult neurodegenerative disease. In some families mitochondrial myopathy has found some members with deafness and diabetes in others strokes along with a mixture of other symptoms. As well as the history and physical examination, blood and urine specialised tests together with brain CT or MRI scanning and skin and muscle biopsy are often needed to make a diagnosis. Patients should be referred as soon as possible to a specialist centre with expertise in metabolic and mitochondrial diseases.

What Treatments are available? (1)

In 2000 treatments for mitochondrial diseases are not very effective. Some effects of these diseases can be treated such as cardiac arrhythmia, seizure disorders, renal bicarbonate loss and hypoglycemia.

When lactic acid accumulation seems to be a major problem an experimental drug dichloroacete DCA, will lower the lactic acid. Although conclusive evidence of efficacy is not yet available, most doctors working with mitochondrial diseases treat there patients with cofactors and vitamins, which are thought to help impaired metabolic pathways. These treatments include combinations of Coenzyme Q10, L-Carnitine, Niacin, Thiamin, Biotin and Riboflavin. Special diets can be helpful.

Some patients benefit by high fat diets with restriction of simple carbohydrates. Fructose restriction may help.

Other patients need high carbohydrate intake with particular supplementation of complex carbohydrates such as uncooked cornstarch.

Only with a through medical evaluation, best carried out in a centre specialising in metabolic & mitochondrial diseases, can the optimal treatment regime for each patient be chosen.

What does the future hold? (1a)

There is no convincing evidence to date of any clear benefit of drug therapies in most archetypal mitochondrial disorders or those neurodegenerative conditions with evidence of mitochondrial dysfunction, and therefore attention has turned to the development of genetic therapies and the possibility of neuroprotection.

New horizons and hopes may lie with genetic strategies. Techniques for manipulating the mitochondrial genome are now being investigated. Whereas nuclear manipulation would necessitate treatment for life, manipulation of the mitochondrial genome would result in a one-off treatment thus providing a "CURE" for Mitochondrial Disorders.

The Children's Mitochondrial Disease Network, is working towards a CURE, with your help, support & increased understanding, this may one day be possible.

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Mitochondrial Disorders: Information Provided & Represented By The Children's Mitochondrial Disease Network

Alpers Disease
Barth Syndrome ***(Cardiomyopthy)***
Carnitine Deficiency
Kearns-Sayre Syndrome ***(KSS)***
Lactic Acidosis
Lethal Infantile Mitochondrial Disease ***(LIMD)***
Leigh's Disease / Syndrome ***(LD & LS)***
Luft Disease
Leber's Hereditary Optic Neuropathy ***(LHON)***
Mitochondrial Cytopathy, Encephalomyopathy & Myopathy: Child & Adult
Mitochondrial DNA ***(mtDNA)*** *Deletions, Ponint Mutations & Depletions*
Nuclear DNA ***(nDNA****) Encoded Defects*
Myoclonic Epilepsy & Ragged - Red Fibres ***(MERRF****)*
Mitochondrial Encephalomyopathy, Lactic Acidosis & Stroke-Like Episodes ***(MELAS)***
Neuropathy, Ataxia & Retinitis Pigmentosa ***(NARP)***
Progressive External Ophthalmolgia ***(PEO)***
Pearson Marrow Syndrome
Cytochrome C Oxidase Deficiency Type A, B, & C ***(COX)***
Pyruvate Dehydrogenase Deficiency & Complex E1 & E2 ***(PDH)***
Pyruvate Carboxylase Deficiency ***(PCH)***
Phosphoenolpruvate Carbokinase Deficiency ***(PEPCK)***
Respiratory Chain Deficiencies: *Complex's I, II, III, IV & V*
Combination's of Complex I, II, III, IV & V
Hypertrophic Cardiomyopathy ***(HCM)***
Mitochondrial Fatty Oxidation Disorders: ***(VLCAD), (MCAD),(SCAD) (LCAD),(MCHAD),(CPT I & II),(ETF),(GAII & MADD),(HMG)***
Oxidative Phosporylation Diseases,
MENKES *Disease,* ***MINGIE*** *Disease*

As our knowledge increases this list is will be expanded accordingly, please do advise if you feel we have missed or possibly overlooked a particular *Mitochondrial* disorder or condition.